35 U.S.C. 1.132 DECLARATION

I, Andrew Lennard Lewis, a UK citizen of Biocompatibles UK Limited, Chapman House, Farnham Business Park, Weydon Lane, Farnham, Surrey GU9 8QL, UK, declare as follows:

1.   I am one of the inventors of this Application. I am currently the Research and Technology Director of Biocompatibles UK Limited ("Biocompatibles"), the assignee of the present Application. I have been at Biocompatibles since 1996, in various roles as Project Manager and Head of Chemistry of the Biomaterials Development Group. I have read the Official Action dated 6 March 2009, and the documents mentioned in that letter.

2.   In Section 5 of the Official Action the Examiner objects that the pending claims in the present Application are unpatentable over co-pending Application No. 10/542333 in view of Storch et al., WO9822517. This objection is based on an interpretation of Storch that that document "teaches that polymer and block copolymers of the type claimed are capable of trapping heparin, negatively charged molecule." The Examiner cites in particular the abstract and pages 5 and 7 of Storch. However Storch does not disclose block copolymers at all, let alone block copolymers within the scope of the pending claims of the present Application. Storch describes copolymers, that is polymers formed from two different monomers but he does not describe the subgroup of copolymers called block copolymers. In Storch, the copolymer is formed essentially from zwitterionic monomer and a cationic monomer. Optionally, a third monomer, also called a termonomer, is included. In the field of polymer technology, copolymers are classified based on how the units derived from the different comonomers are arranged along the polymer chain. Among different types of copolymers are the categories 1) alternating copolymers, 2) random copolymers and 3) block copolymers (see supporting Figure 1). Alternating copolymers have alternating units derived from a first comonomer and a second comonomer (Figure 1-1). Random copolymers, sometimes called statistical copolymers, have a random sequence of units derived from the different comonomers (Figure 1-2). Block copolymers comprise two or more polymer portions (usually homopolymer) linked by covalent bonds (Figure 1-3).

3.   An alternating copolymer will always have about equimolar amounts of units derived from the two monomers. Random copolymers and block copolymers can have any of a broad range of molar ratios between the comonomers. For a random

copolymer, where the ratio of units derived from one comonomer to units derived from the other comonomer is 1:2, a polymer chain will have a random arrangement which has on average twice as many units derived from the second comonomer as the first comonomer. A block copolymer having a molar ratio of 1:2 will have a first block formed of a homopolymer of the first comonomer and a second block which is a homopolymer of the second comonomer formed of twice as many units of that comonomer. Random copolymers are formed when both comonomers are present when polymerisation is initiated, assuming that the monomers are copolymerisable with one another under the polymerisation conditions. Block copolymers are made by polymerising the first comonomer at a different time to the second comonomer. For instance the first block may be formed in a first step in which homopolymer of the first comonomer is formed, the second comonomer not being present then polymerisation to form the second block is carried out in a second step by addition of the second comonomer to the first stage product mixture under conditions such that polymerisation takes place from the chain ends of homopolymer formed of the first comonomer. Alternatively, preformed blocks of the first comonomer may be grafted with homopolymer formed of the second comonomer.

4.   Both random copolymers and block copolymers may be represented by listing the comonomers from which the copolymer is formed and specifying the molar proportion, for instance as a subscript following the comonomer name or abbreviation. For instance, $A_{0.2}B_{08}$ represents a polymer comprising units derived from monomer A and monomer B in molar ratio 0.2:0.8 (1:4). The notation does not define the arrangement of units along a chain. The arrangement, that is whether the polymer is a random copolymer or a block copolymer, may be separately indicated, for instance by a letter B between the monomer names. The letter b means block in this notation. More usually the type of copolymer has to be inferred from the way the polymerisation is conducted. Unless otherwise stated, most polymerisations of ethylenically unsaturated comonomers are random copolymerisations to produce random copolymers.

5.   Storch defines the polymer having pendant zwitterionic and cationic groups as generally being "a copolymer of copolymerisable monomer" (page 6, lines 35-36). The range of zwitterionic to ionic groups is mentioned at page 12, lines 1-3. There is no specific mention regarding the type of process used to form the copolymer until the worked examples. In the worked examples, all of the polymerisations are random copolymerisations (as per Figure 1-4). For instance in Example 1, a terpolymer is formed from a starting mixture containing 40 parts by weight MPC, 71 parts by weigh dodecylmethacrylate and 8 parts by weight cationic monomer. The monomers are combined together in a suitable solvent mixture before initiation of polymerisation. The polymer produced will be a random copolymer. A similar technique is used in Example 2, the only difference being that a different ionic monomer is utilised. In Example 3, two variations of the random copolymerisation technique are used. In 3.1, polymerisation is controlled by continuously feeding monomer into the polymerisation vessel where initiator is present. A mixture of the same ratio of comonomers is used in the polymerisation throughout the monomer feed period, with monomers being premixed before being fed into the polymerisation vessel. In the second, "one-pot" method, all the monomer mixture is included at the start of the polymerisation. The copolymer products of both methods will be random copolymers. In Example 4, the monomer feed and one pot methods are used for forming a five component polymer. Again all monomers are present at the start of polymerisation and in the monomer feed

mixture. Similar techniques are used in Example 5 to produce a terpolymer, again that will be random in nature as depicted in Figure 1-4. None of the polymers produced in Storch et al is a block copolymer as depicted in Figure 1-5. Nor is there any suggestion in Storch that the comonomers could as a variant be polymerised in such a manner as to produce block copolymers. Block copolymers are not mentioned in Storch.

6.   In Sections 9 and 10 of the Official Action the Examiner rejects some of the claims in view of Stratford WO0028920. Again the Examiner indicates that "Stratford teaches the polymer of the type claimed". Stratford 1920 describes copolymers formed of zwitterionic monomer and ionic comonomer. The polymer is formed by radical polymerisation of ethylenically unsaturated monomers including the zwitterionic monomer and the ionic monomer, that is the monomers are polymerised together and will form a random copolymer. A specific example of copolymerisation is given in Example 1. At page 13, lines 18-20, it is explained that all the comonomers are dissolved together into a suitable solvent. In the tables, the comonomers are defined by reference to the weight proportions of the monomers in the mixture. All of the polymers are made in the same manner, that is by random copolymerisation to produce polymers as per Figure 1-4. Stratford 1920 does not mention the block copolymers nor any polymerisation method that will form block copolymers as per Figure 1-5.

7.   In paragraphs 13 and 14, the Examiner rejects the pending claims as being obvious over Stratford et al., WO0029481 in view of Storch. The disclosure of Stratford '481 is very similar to that of Stratford '920. There is no additional general description of copolymers which suggests that block copolymers could be used. The way the polymer is described in Stratford '481 indicates that the comonomers are mixed before polymerisation, and the worked examples are consistent with this. The worked examples indeed are identical to those described in Stratford '920, inevitably forming random copolymers.

8.   In Sections 15 and 16 of the Official Action, the Examiner rejects the pending claims as being unpatentable over Stratford '481 in view of Koulik et al. The Examiner suggests that "Koulik teaches a terpolymer of MPC, alkylacrylate and aminoethylacrylate". The Examiner is correct in this assertion. However the Examiner is not correct in his statement that "the terpolymer of Koulik .....meet(s) the polymer limitations of claims 1, 8-22, 28-34". The Examiner directs attention in particular to column 6, lines 4-40 of Koulik. These passages refer to the "block representation of a suitable copolymer coating" used in the invention of Koulik, illustrated in Figure 1b. Figure 1b is a schematic representation of the terpolymer shown in the chemical structure in Figure 1c. In Figure 1c, units derived from the three monomers, MPC, butylmethacrylate and 2-aminoethylmethacrylate are shown, in the molar ratios a:b:c. Figure 1b indicates that the butylmethacrylate derived unit has a hydrophobic group, the MPC-derived unit has a hydrophilic group, and the 2-aminoethylmethacrylate-derived unit has a functional group. However these diagrams do not illustrate a block copolymer specifically. They simply illustrate a terpolymer formed of the three monomer units. Although Koulik uses the term "block", this defines the representation, i.e. the figure in the patent specification, and not the polymer itself.

9.   In order to determine whether the terpolymer described in Koulik is a random copolymer or a block copolymer, it is necessary to consider the polymerisation

methods described. At column 7, from line 5, and in corresponding Figure 3, Koulik describes initially forming "an acceptable mixture of hydrophobic monomer/hydrophilic monomer/functional monomer". The relative molar proportions are given at line 20. Again the selected monomers are mixed at step 122 in Figure 3 and then polymerised, in the subsequent step schematically illustrated as step 124 in Figure 3. Since all of the monomers are mixed before polymerisation is conducted, a random terpolymer will be formed as per Figure 1-4. This is confirmed in the worked Examples where the three monomers are dissolved together into ethanol before initiator is added to initiate polymerisation.

10.   I acknowledge that willful false statements and the like are punishable by fine or imprisonment or both (18 U.S.C. 1001) and may jeopardise the validity of the Application or any Patent issuing thereon. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true.

Dated this 28th day of   A P R I L   2009
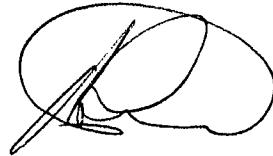
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Figure 1: Copolymer Types
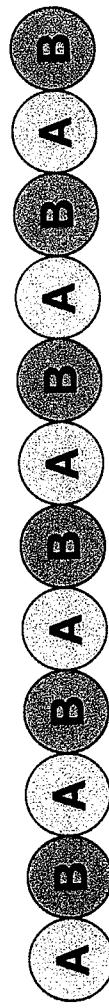
1) AB alternating copolymer

2) AB random/statistical copolymer (A-*co*-B)
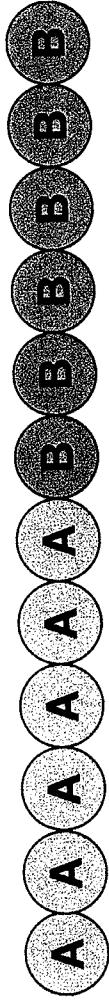
3) AB block copolymer (A-*b*-B)
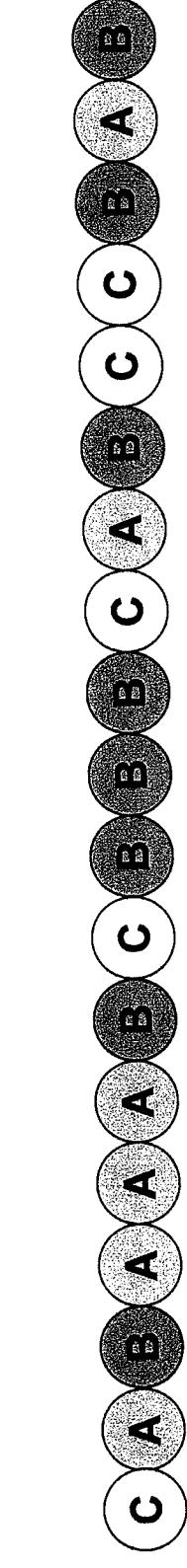
4) ABC random terpolymer

5) ABC block terpolymer